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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,703	10/31/2003	H. William Bosch	029318-0973	8369

31049 7590 10/23/2009

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EXAMINER	
CLARK, SARA E	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
10/23/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/697,703	BOSCH ET AL.	
	Examiner	Art Unit	
	SARA E. CLARK	1612	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 08 October 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1-31,36-38,40 and 44*.
   Claim(s) withdrawn from consideration: *32-35,39,41-43 and 45-95*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☒ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). 10/8/2009
13. ☒ Other: See Continuation Sheet.

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612

/SARA E. CLARK/
AU 1612

Continuation of 11. does NOT place the application in condition for allowance because: Applicant contends that Reiner's teaching of nimesulide drug particles "in the micron size range" does not teach or suggest the limitation particles having an "effective average particle size of less than 2000 nm" (2 microns), as recited by claim 1, but rather particles ranging in size from 1 to 999 microns. However, "in the micron size range" reasonably suggests particles in the size range of one micron, particularly considering that (a) the drug particles of Reiner are sprayed onto the surface of sugary microgranules having a size of 850 microns, so that by implication, the relative size of the drug particles must be much smaller than the sugary microgranules onto which they are coated, and (b) the plain meaning of "micronized" connotes "to pulverize, especially into particles a few micrometers [microns] in diameter" (Merriam-Webster online dictionary, accessed 10/17/2009). In addition, Ryde discloses nanoparticulate compositions in which the active agent has an effective average particle size of less than about one micron (col. 6, lines 23-51).

Applicant further contends that there is no rationale to combine Reiner and Ryde, because the two references are directed to unrelated technologies and could be combined to arrive at the claimed invention only by impermissible hindsight. However, both Reiner and Ryde disclose solid-dose nanoparticle pharmaceutical compositions formulated for oral administration of poorly soluble active agents. Improving a drug's pharmacokinetic profile, such as its dispersibility and bioavailability, is a common objective in the pharmaceutical arts, which can be achieved by making one or more of several well-known modifications. These include, for example, reducing particle size to increase surface area, and formulation with certain excipients to enhance the drug's solubility. Thus, optimizing the particle size and choice of excipient(s) involves routine experimentation rather than an inventive step, particularly when the adjustments have been attempted and proven useful in similar drug formulations, as in Reiner and Ryde.

Finally, Applicant contends that modifying Reiner in view of Ryde would destroy the intended purpose of a component in Reiner, or alternatively, that there is no teaching in either of the cited references that micron-sized drug particles need surface stabilizers to prevent aggregation. However, as noted in the previous Office Action, Ryde teaches that a frequent problem in prior art nanoparticulate compositions was that upon administration to a mammal, the nanoparticulate composition fails to redisperse and forms clumps or agglomerated drug particles, reducing the drug's bioavailability (col. 5, lines 31-45), and that an improvement taught in some prior art patents is the usefulness of polymeric surface stabilizers for nanoparticulate compositions (col. 3, lines 39-53).

In light of the foregoing, no impermissible hindsight is required to arrive at a pharmaceutical composition comprising nimesulide particles having an average effective particle size of less than 2 microns with at least one surface stabilizer adsorbed onto the surface thereof, as recited by the instant claims. Hence, the rejections of claims 1-31, 36-38, 40, and 44 are maintained. .

Continuation of 13. Other: The IDS dated 10/8/2009 was not considered because it fails to meet the requirements of MPEP 609 as set forth in 37 CFR 1.97(e).